CuBr for KA² Reaction: En Route to Propargylic Amines Bearing a Quaternary Carbon Center

Xinjun Tang, Jinqiang Kuang, and Shengming Ma

State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Lingling Lu, Shanghai 200032, P. R. China

Shanghai Key Laboratory of Green Chemistry and Chemical Process, Department of Chemistry, East China Normal University, 3663 North Zhongshan Road, Shanghai 200062, P. R. China

Fax: (+86)21-62609305; Email: masm@sioc.ac.cn

Supporting Information

Index

1. Typical Procedure and Analytical Data for Compounds 4a-4r
2. ¹H NMR and ¹³C NMR Spectra for Compounds 4a-4r
3. Reference

S2
S15
S55
**General Information.** All reactions were carried out in oven dried Schlenk vessels. CuBr (99.0%) was purchased from Aladdin and kept in glove box. 4 Å molecular sieves was purchased from Alfa Aesar and kept in glove box after activation (heated at 450 °C for 10 h in Muffle furnace, taken out after cooling to 200 °C and then kept in a glove box to allow to cool to room temperature) under N₂. Toluene was dried over sodium wire with benzophenone as the indicator and distilled freshly before use. Anhydrous benzene was purchased from Aladdin and used without further treatment. Other reagents were used without further treatment. All the temperatures are referred to the oil baths used.

(1) 1-(3-Methyl-1-phenylhept-1-yn-3-yl)pyrrolidine 4a (tangxj-4-141)

![Chemical Structure](image)

Typical Procedure 1: To a dried Schlenk tube was added 4 Å MS (3.0012 g) inside a glove box. The Schlenk tube was then dried under vacuum with a heating gun. CuBr (0.0218 g, 0.15 mmol), 1a (1.0211 g, 10 mmol)/toluene (3 mL), 2a (1.1025 g, 11 mmol)/toluene (3 mL), and 3a (0.7824 g, 11 mmol)/toluene (4 mL) were then added sequentially under Ar atmosphere. The Schlenk tube was then placed in a pre-heated oil bath at 100 °C with stirring for 1 h as monitored by TLC. After cooling to room temperature, the crude reaction mixture was filtrated through a short pad of silica gel eluted with acetone (50 mL). After evaporation, the residue was analyzed by ¹H NMR measurement with 70 µL of mesitylene added as the reference and then purified via chromatography on silica gel to afford 4a (2.3577 g, 92%) (eluent: petroleum ether (200 mL); then petroleum ether/ethyl acetate = 150/1 (200 mL); finally petroleum ether/ethyl acetate/Et₃N = 900 mL/180 mL/1 mL was applied to get the pure product.) as a liquid: ¹H NMR (400 MHz, CDCl₃) δ 7.44-7.38 (m, 2 H, Ar-H), 7.29-7.19 (m, 3 H, Ar-H), 2.84-2.72 (m, 4 H, CH₂NCH₂), 1.85-1.72 (m, 5 H, 2×CH₂ + one proton of
CH₂), 1.72-1.62 (m, 1 H, one proton of CH₂), 1.56-1.27 (m, 7 H, 2×CH₂ + CH₃), 0.94 (t, J = 7.2 Hz, 3 H, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 131.5, 127.9, 127.4, 123.5, 91.2, 84.2, 57.6, 47.6, 41.1, 26.3, 25.7, 23.5, 23.0, 14.0; MS (ESI) m/z 256 (M+H⁺), 185 (M+H⁺-pyrrolidine); IR (neat): ν = 2956, 2870, 2807, 1598, 1489, 1463, 1444, 1370, 1334, 1302, 1190, 1144, 1091, 1069, 1000 cm⁻¹; HRMS calcd for C₁₈H₂₅N [M⁺]: 255.1987. Found: 255.1989.

The following compounds were prepared according to this Typical Procedure.

(2) 1-(1-(4-Methoxyphenyl)-3-methylhept-1-yn-3-yl)pyrrolidine 4b (tangxj-4-151)

The reaction of 4 Å MS (2.9979 g), CuBr (0.0212 g, 0.15 mmol), 1b (1.3452 g, 10 mmol), 2a (1.1018 g, 11 mmol)/toluene (5 mL), and 3a (0.7825 g, 11 mmol)/toluene (5 mL) afforded 4b (2.5084 g, 86%) (eluuent: petroleum ether (200 mL); then petroleum ether/ethyl acetate = 150/1 (200 mL); finally petroleum ether/ethyl acetate/Et₃N = 900 mL /180 mL /1 mL was applied to get the pure product.) as a liquid: ¹H NMR (400 MHz, CDCl₃) δ 7.35 (d, J = 8.8 Hz, 2 H, Ar-H), 6.81 (d, J = 8.8 Hz, 2 H, Ar-H), 3.78 (s, 3 H, OCH₃), 2.84-2.72 (m, 4 H, CH₂NCH₂), 1.84-1.61 (m, 6 H, 3×CH₂), 1.55-1.28 (m, 7 H, 2×CH₂ + CH₃), 0.93 (t, J = 7.2 Hz, 3 H, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 159.0, 133.0, 115.7, 113.6, 89.7, 83.9, 57.7, 55.1, 47.6, 41.3, 26.5, 25.9, 23.5, 23.1, 14.0; MS (ESI) m/z 286 (M+H⁺), 215 (M+H⁺-pyrrolidine); IR (neat): ν = 2955, 1606, 1508, 1463, 1370, 1335, 1288, 1244, 1169, 1143, 1103, 1001 cm⁻¹; HRMS calcd for C₁₉H₂₇NO [M⁺]: 285.2093. Found: 285.2088.

(3) 1-(1-(4-Bromophenyl)-3-methylhept-1-yn-3-yl)pyrrolidine 4c (tangxj-4-144)
The reaction of 4 Å MS (3.0015 g), CuBr (0.0218 g, 0.15 mmol), 1c (1.8014 g, 10 mmol)/toluene (3 mL), 2a (1.1018 g, 11 mmol)/toluene (3 mL), and 3a (0.7831 g, 11 mmol)/toluene (4 mL) afforded 4c (2.9007 g, 87%) (eluent: petroleum ether (200 mL); then petroleum ether/ethyl acetate = 150/1 (200 mL); finally petroleum ether/ethyl acetate/Et3N = 900 mL/180 mL/1 mL was applied to get the pure product.) as a liquid: 1H NMR (400 MHz, CDCl3) δ 7.40 (d, J = 8.4 Hz, 2 H, Ar-H), 7.26 (d, J = 8.0 Hz, 2 H, Ar-H), 2.82-2.70 (m, 4 H, CH2NCH2), 1.82-1.62 (m, 6 H, 3 × CH2), 1.52-1.28 (m, 7 H, 2 × CH2 + CH3), 0.93 (t, J = 7.2 Hz, 3 H, CH3); 13C NMR (100 MHz, CDCl3) δ 133.1, 131.3, 122.4, 121.6, 92.7, 83.2, 57.8, 47.7, 41.1, 26.4, 25.7, 23.5, 23.1, 14.0; MS (ESI) m/z 336 (M(81Br)+H+), 334 (M(79Br)+H+), 265 (M(81Br)+H+)-pyrrolidine), 263 (M(79Br)+H+)-pyrrolidine); IR (neat): ν = 2956, 2869, 2807, 1484, 1462, 1392, 1370, 1262, 1145, 1093, 1069, 1010 cm⁻¹; HRMS calcd for C18H2479BrN [M⁺]: 333.1092. Found: 333.1102.

(4) 1-(1-(3-Bromophenyl)-3-methylhept-1-yn-3-yl)pyrrolidine 4d (tangxj-4-154)

The reaction of 4 Å MS (3.0025 g), CuBr (0.0214 g, 0.15 mmol), 1d (1.8002 g, 10 mmol)/toluene (3 mL), 2a (1.1010 g, 11 mmol)/toluene (3 mL), and 3a (0.7831 g, 11 mmol)/toluene (4 mL) afforded 4d (2.9954 g, 90%) (eluent: petroleum ether (200 mL); then petroleum ether/ethyl acetate = 150/1 (200 mL); finally petroleum ether/ethyl acetate/Et3N = 900 mL/180 mL/1 mL was applied to get the pure product.) as a liquid: 1H NMR (400 MHz, CDCl3) δ 7.56 (s, 1 H, Ar-H), 7.39 (d, J = 7.2 Hz, 1 H,
Ar-H), 7.33 (d, J = 7.6 Hz, 1 H, Ar-H), 7.15 (t, J = 7.8 Hz, 1 H, Ar-H), 2.82-2.72 (m, 4 H, CH₂NCH₂), 1.86-1.61 (m, 6 H, 3 × CH₂), 1.52-1.30 (m, 7 H, 2 × CH₂ + CH₃), 0.94 (t, J = 7.2 Hz, 3 H, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 134.2, 130.5, 130.0, 129.3, 125.4, 121.8, 92.9, 82.7, 75.6, 47.5, 40.9, 26.2, 25.6, 23.4, 23.0, 13.9; MS (ESI) m/z 336 (M(⁸¹Br)+H⁺), 334 (M(⁷⁹Br)+H⁺); IR (neat): ν = 2956, 2870, 2807, 1589, 1555, 1470, 1404, 1119, 1069, 1039 cm⁻¹; HRMS calcd for C₁₈H₂₄⁷⁹BrN [M⁺]: 333.1092. Found: 333.1085.

(5) 1-(1-(2-Chlorophenyl)-3-methylhept-1-yn-3-yl)pyrrolidine 4e (tangxj-4-155)

The reaction of 4 Å MS (3.0011 g), CuBr (0.0211 g, 0.15 mmol), 1e (1.3602 g, 10 mmol)/toluene (3 mL), 2a (1.1015 g, 11 mmol)/toluene (3 mL), and 3a (0.7821 g, 11 mmol)/toluene (4 mL) afforded 4e (2.6450 g, 92%) (eluent: petroleum ether (200 mL); then petroleum ether/ethyl acetate = 180/1 (200 mL); finally petroleum ether/ethyl acetate/Et₃N = 900 mL /180 mL /1 mL was applied to get the pure product.) as a liquid: ¹H NMR (400 MHz, CDCl₃) δ 7.47-7.41 (m, 1 H, Ar-H), 7.39-7.32 (m, 1 H, Ar-H), 7.21-7.11 (m, 2 H, Ar-H), 2.88-2.75 (m, 4 H, CH₂NCH₂), 1.86-1.65 (m, 6 H, 3 × CH₂), 1.60-1.29 (m, 7 H, 2 × CH₂ + CH₃), 0.94 (t, J = 7.2 Hz, 3 H, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 135.6, 133.1, 128.9, 128.4, 126.1, 123.3, 97.2, 80.9, 58.1, 47.6, 41.0, 26.4, 25.7, 23.6, 23.0, 14.0; MS (ESI) m/z 292 (M(³⁷Cl)+H⁺), 290 (M(³⁵Cl)+H⁺), 219 (M(³⁵Cl)+H⁺-pyrrolidine); IR (neat): ν = 2956, 2870, 2810, 2221, 1470, 1437, 1370, 1146, 1057, 1033, 1000 cm⁻¹; HRMS calcd for C₁₈H₂₄³⁵ClN [M⁺]: 289.1597. Found: 289.1594.

(6) 1-(5-Methyltridec-6-yn-5-yl)pyrrolidine 4f (tangxj-4-147)
The reaction of 4 Å MS (3.0021 g), CuBr (0.0219 g, 0.15 mmol), 1f (1.1038 g, 10 mmol)/toluene (3 mL), 2a (1.1021 g, 11 mmol)/toluene (3 mL), and 3a (0.7823 g, 11 mmol)/toluene (4 mL) afforded 4f (2.2463 g, 85%) (eluent: petroleum ether (200 mL); then petroleum ether/ethyl acetate = 150/1 (200 mL); finally petroleum ether/ethyl acetate/Et₃N = 900 mL/180 mL/1 mL was applied to get the pure product.) as a liquid: 1H NMR (400 MHz, CDCl₃) δ 2.76-2.62 (m, 4 H, CH₂NCH₂), 2.19 (t, J = 6.6 Hz, 2 H, CH₂C≡C), 1.82-1.72 (m, 4 H, 2×CH₂), 1.69-1.22 (m, 17 H, 7×CH₂ + CH₃), 0.95-0.85 (m, 6 H, 2×CH₃); 13C NMR (100 MHz, CDCl₃) δ 83.9, 81.2, 57.3, 47.4, 41.5, 31.2, 29.1, 28.3, 26.5, 26.0, 23.5, 23.1, 22.5, 18.5, 14.0, 13.9; MS (ESI) m/z 264 (M+H⁺); IR (neat): ν = 2956, 2930, 2859, 2809, 1463, 1370, 1303, 1260, 1237, 1175 cm⁻¹; HRMS calcd for C₁₈H₃₃N [M⁺]: 263.2613. Found: 263.2603.

(7) 2,5-Dimethyl-5-(pyrrolidin-1-yl)non-3-yn-2-ol 4g (tangxj-4-164)

The reaction of 4 Å MS (2.9979 g), CuBr (0.0214 g, 0.15 mmol), 1g (0.8409 g, 10 mmol)/toluene (3 mL), 2a (1.1033 g, 11 mmol)/toluene (3 mL), and 3a (0.7821 g, 11 mmol)/toluene (4 mL) afforded 4g (2.0509 g, 86%) (eluent: petroleum ether (200 mL); then petroleum ether/ethyl acetate = 50/1 (200 mL)→1/1 (200 mL); finally petroleum ether/ethyl acetate/Et₃N = 180 mL/900 mL/1 mL was applied to get the pure product.): solid; m.p. 53-55 °C (ethyl ether/petroleum ether); 1H NMR (400 MHz, CDCl₃) δ 2.73-2.62 (m, 4 H, CH₂NCH₂), 2.23 (br s, 1 H, OH), 1.81-1.72 (m, 4 H, 2×CH₂), 1.69-1.53 (m, 2 H, CH₂), 1.52 (s, 6 H, 2×CH₃), 1.43-1.25 (m, 7 H, 2×CH₂+CH₃), 0.91 (t, J = 7.0 Hz, 3 H, CH₃); 13C NMR (100 MHz, CDCl₃) δ 89.1, 83.3, 65.1, 57.1, 47.5, 41.0, 32.03, 32.00, 26.5, 25.7, 23.6, 23.1, 14.1; MS (ESI) m/z 238 (M+H⁺);
IR (neat): $\nu = 3132, 2987, 2951, 2926, 2871, 2833, 1470, 1455, 1372, 1246, 1219, 1173, 1145, 1090$ cm$^{-1}$; Anal. Calcd for $C_{13}$H$_{27}$NO: C 75.90, H 11.46, N 5.90. Found: C 75.86, H 11.30, N 5.88.

(8) 1-[[1-((tert-Butyldimethylsilyl)oxy)-4-methyloct-2-yn-4-yl]pyrrolidine $4h$

The reaction of $4$ Å MS (3.0008 g), CuBr (0.0218 g, 0.15 mmol), $1h$ (1.7032 g, 10 mmol)/toluene (3 mL), $2a$ (1.1021 g, 11 mmol)/toluene (3 mL), and $3a$ (0.7829 g, 11 mmol)/toluene (4 mL) afforded $4h$ (2.5337 g, 78%) (eluent: petroleum ether/ethyl acetate = 150/1 (200 mL) $\rightarrow$ 50/1 (200 mL); finally petroleum ether/ethyl acetate/Et$_3$N = 900 mL /180 mL /1 mL was applied to get the pure product.) as a liquid: $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 4.36 (s, 2 H, OCH$_2$), 2.76-2.65 (m, 4 H, CH$_2$NCH$_2$), 1.81-1.73 (m, 4 H, 2$\times$CH$_2$), 1.71-1.52 (m, 2 H, CH$_2$), 1.48-1.24 (m, 7 H, 2$\times$CH$_2$ + CH$_3$), 0.94-0.88 (m, 12 H, 4$\times$CH$_3$), 0.13 (s, 6 H, CH$_3$SiCH$_3$); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 86.2, 82.7, 57.3, 51.7, 47.5, 41.1, 26.4, 25.72, 25.70, 23.5, 23.1, 18.2, 14.0, -5.1; MS (ESI) m/z 324 (M+H$^+$); IR (neat): $\nu = 2956, 2931, 2859, 1464, 1368, 1253, 1092, 1001$ cm$^{-1}$; HRMS calcd for $C_{19}$H$_{37}$NOSi [M$^+$]: 323.2644. Found: 323.2638.

(9) 1-[[3-Methyl-1-phenylpent-1-yn-3-yl]pyrrolidine $4i$ (tangxj-4-156)

The reaction of $4$ Å MS (3.0024 g), CuBr (0.0213 g, 0.15 mmol), $1a$ (1.0205 g, 10 mmol)/toluene (3 mL), $2b$ (0.7974 g, 11 mmol)/toluene (3 mL), and $3a$ (0.7818 g, 11 mmol)/toluene (4 mL) afforded $4i$ (1.9747 g, 87%) (eluent: petroleum ether (200 mL); then petroleum ether/ethyl acetate = 150/1 (200 mL); finally petroleum ether/ethyl...
acetate/Et$_3$N = 900 mL /180 mL /1 mL was applied to get the pure product.) as a liquid: $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.46-7.35 (m, 2 H, Ar-H), 7.28-7.18 (m, 3 H, Ar-H), 2.84-2.70 (m, 4 H, CH$_2$NCH$_2$), 1.90-1.74 (m, 5 H, 2$\times$CH$_2$ + one proton of CH$_2$), 1.74-1.62 (m, 1 H, one proton of CH$_2$), 1.41 (s, 3 H, CH$_3$), 1.04 (t, $J = 7.4$ Hz, 3 H, CH$_3$); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 131.4, 127.9, 127.3, 123.4, 90.9, 84.3, 58.1, 47.5, 33.8, 25.0, 23.4, 8.7; MS (ESI) m/z 228 (M+H$^+$), 157 (M+H$^+$-pyrrolidine); IR (neat): $\nu = $ 2967, 2936, 2874, 2807, 1598, 1488, 1460, 1444, 1369, 1292, 1174, 1145 cm$^{-1}$; HRMS calcd for C$_{16}$H$_{21}$N [M$^+$]: 227.1674. Found: 227.1674.

(10) 1-(3-Methyl-1-phenylnon-1-yn-3-yl)pyrrolidine 4j (tangxj-4-142)

$$\begin{align*}
\text{Ph} & \quad + \quad \text{H}_3\text{C}^+\text{N}_3\text{C}_8\text{H}_{13} \quad + \quad \text{CuBr (1.5 mol%)} \quad \text{4 Å MS} \quad \text{toluene, 100 °C} \\
\text{1a} & \quad 1.1 \text{ equiv} \quad 2c & \quad 1.1 \text{ equiv} \quad 3a & \quad \rightarrow \quad \text{Ph} & \quad + \quad \text{nC}_6\text{H}_{13} \quad \text{4j}
\end{align*}$$

The reaction of 4 Å MS (3.0021 g), CuBr (0.0210 g, 0.15 mmol), 1a (1.0221 g, 10 mmol)/toluene (3 mL), 2c (1.4098 g, 11 mmol)/toluene (3 mL), and 3a (0.7825 g, 11 mmol)/toluene (4 mL) afforded 4j (2.4298 g, 86%) (eluent: petroleum ether (200 mL); then petroleum ether/ethyl acetate = 150/1 (200 mL); finally petroleum ether/ethyl acetate/Et$_3$N = 900 mL /180 mL /1 mL was applied to get the pure product.) as a liquid: $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.44-7.37 (m, 2 H, Ar-H), 7.30-7.21 (m, 3 H, Ar-H), 2.85-2.71 (m, 4 H, CH$_2$NCH$_2$), 1.84-1.61 (m, 6 H, 3$\times$CH$_2$), 1.55-1.41 (m, 5 H, CH$_2$ + CH$_3$), 1.36-1.27 (m, 6 H, 3$\times$CH$_2$), 0.89 (t, $J = 6.6$ Hz, 3 H, CH$_3$); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 131.6, 128.0, 127.5, 123.5, 91.3, 84.2, 57.7, 47.6, 41.4, 31.7, 29.7, 25.8, 24.2, 23.5, 22.6, 14.0; MS (ESI) m/z 284 (M+H$^+$), 256 (M+H$^+$-CH$_2$=CH$_2$), 213 (M+H$^+$-pyrrolidine); IR (neat): $\nu = $ 2928, 2869, 2808, 1573, 1489, 1463, 1370, 1102, 1070, 1026 cm$^{-1}$; HRMS calcd for C$_{20}$H$_{29}$N [M$^+$]: 283.2300. Found: 283.2303.

(11) 1-(3-Methyl-1,5-diphenylpent-1-yn-3-yl)pyrrolidine 4k (tangxj-4-157)
The reaction of 4 Å MS (3.0032 g), CuBr (0.0216 g, 0.15 mmol), 1a (1.0208 g, 10 mmol)/toluene (3 mL), 2d (1.6300 g, 11 mmol)/toluene (3 mL), and 3a (0.7831 g, 11 mmol)/toluene (4 mL) afforded 4k (2.7098 g, 89%) (eluent: petroleum ether (200 ml); then petroleum ether/ethyl acetate = 150/1 (200 mL) → 100/1 (200 mL); finally petroleum ether/ethyl acetate/Et₃N = 900 mL/180 mL/1 mL was applied to get the pure product.) As a liquid: ¹H NMR (400 MHz, CDCl₃) δ 7.46-7.38 (m, 2 H, Ar-H), 7.32-7.11 (m, 8 H, Ar-H), 2.87-2.73 (m, 6 H, CH₂NCH₂+CH₂), 2.16-1.96 (m, 2 H, CH₂), 1.86-1.74 (m, 4 H, 2×CH₂), 1.53 (s, 3 H, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 142.4, 131.6, 128.3, 128.2, 127.6, 125.6, 123.3, 90.9, 84.6, 57.6, 47.7, 43.3, 30.7, 25.7, 23.6; MS (ESI) m/z 304 (M+H⁺), 233 (M+H⁺-pyrrolidine); IR (neat): v = 2961, 2871, 2807, 1599, 1490, 1454, 1370, 1276, 1130 cm⁻¹; HRMS calcd for C₂₂H₂₅N [M⁺]: 303.1987. Found: 303.1980.

(12) 1-(3,4-Dimethyl-1-phenylpent-1-yn-3-yl)pyrrolidine 4l (tangxj-4-176)

The reaction of 4 Å MS (3.0012 g), CuBr (0.0216 g, 0.15 mmol), 1a (1.0205 g, 10 mmol) /toluene (3 mL), 2e (0.9472 g, 11 mmol)/toluene (3 mL), and 3a (0.7824 g, 11 mmol)/toluene (4 mL) afforded 4l (1.9375 g, 80%) (eluent: petroleum ether (200 mL); then petroleum ether/ethyl acetate = 100/1 (200 mL) → 100/1 (200 mL); finally petroleum ether/ethyl acetate/Et₃N = 900 mL/180 mL/1 mL was applied to get the pure product.) As a liquid: ¹H NMR (400 MHz, CDCl₃) δ 7.45-7.36 (m, 2 H, Ar-H), 7.31-7.23 (m, 3 H, Ar-H), 2.81-2.68 (m, 4 H, CH₂NCH₂), 2.06 (heptet, J = 6.8 Hz, 1 H, CH), 1.83-1.70 (m, 4 H, 2×CH₂), 1.25 (s, 3 H, CH₃), 1.11 (d, J = 6.8 Hz, 3 H,
CH₃), 0.94 (d, J = 7.2 Hz, 3 H, CH₃); ^{13}C NMR (100 MHz, CDCl₃) δ 131.6, 128.1, 127.5, 123.7, 91.9, 84.4, 61.5, 47.3, 35.1, 23.6, 19.4, 19.1, 15.5; MS (ESI) m/z 242 (M+H⁺), 171 (M+H⁺-pyrrolidine); IR (neat): ν = 2963, 2873, 2807, 1598, 1490, 1463, 1444, 1384, 1367, 1254, 1194, 1160, 1140 cm⁻¹; HRMS calcd for C₁₇H₂₃N [M⁺]: 241.1830. Found: 241.1833.

(13) 1-(3-Ethyl-1-phenylhex-1-yn-3-yl)pyrrolidine 4m (tangxj-4-173)

The reaction of 4 Å MS (3.0018 g), CuBr (0.0218 g, 0.15 mmol), 1a (1.0205 g, 10 mmol) /toluene (3 mL), 2f (1.1009 g, 11 mmol)/toluene (3 mL), and 3a (0.7824 g, 11 mmol)/toluene (4 mL) afforded 4m (2.1310 g, 84%) (eluent: petroleum ether (200 mL); then petroleum ether/ethyl acetate = 100/1 (200 mL) → 50/1 (200 mL); finally petroleum ether/ethyl acetate/Et₃N = 900 mL/180 mL/1 mL was applied to get the pure product.) as a liquid: ^{1}H NMR (400 MHz, CDCl₃) δ 7.44-7.38 (m, 2 H, Ar-H), 7.30-7.22 (m, 3 H, Ar-H), 2.80-2.70 (m, 4 H, CH₂NCH₂), 1.85-1.62 (m, 8 H, 4×CH₂), 1.49-1.37 (m, 2 H, CH₂), 0.99-0.92 (m, 6 H, 2×CH₃); ^{13}C NMR (100 MHz, CDCl₃) δ 131.7, 128.1, 127.5, 123.7, 91.5, 84.6, 61.5, 47.3, 38.6, 29.6, 23.6, 16.9, 14.5, 8.2; MS (ESI) m/z 256 (M+H⁺), 185 (M+H⁺-pyrrolidine); IR (neat): ν = 2959, 2873, 2807, 1598, 1489, 1459, 1294, 1259, 1145, 1120, 1069, 1026 cm⁻¹; HRMS calcd for C₁₈H₂₅N [M⁺]: 255.1987. Found: 255.1990.

(14) 1-(4-(Phenylethynyl)heptan-4-yl)pyrrolidine 4n (tangxj-5-22)

The reaction of 4 Å MS (3.0012 g), CuBr (0.0709 g, 0.5 mmol), 1a (1.0201 g, 10 mol)
mmol)/toluene (3 mL), 2g (1.2547 g, 11 mmol)/toluene (3 mL), and 3a (0.7821 g, 11 mmol)/toluene (4 mL) afforded 4n (1.7765 g, 66%) (eluent: petroleum ether (200 mL); then petroleum ether/ethyl acetate = 200/1 (200 mL); finally petroleum ether/ethyl acetate/Et$_3$N = 900 mL/90 mL/1 mL was applied to get the pure product) as a liquid: 
$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.44-7.36 (m, 2 H, Ar-H), 7.30-7.19 (m, 3 H, Ar-H), 2.79-2.69 (m, 4 H, CH$_2$NCH$_2$), 1.82-1.62 (m, 8 H, 4×CH$_2$), 1.51-1.37 (m, 4 H, 2×CH$_2$), 0.94 (t, $J$ = 7.4 Hz, 6 H, 2×CH$_3$); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 131.6, 128.1, 127.5, 123.7, 112.1, 106.8 cm$^{-1}$; HRMS calcd for C$_{19}$H$_{27}$N [M$^+$]: 269.2143. Found: 269.2138.

(15) 1-(1-(Phenylethynyl)cyclohexyl)pyrrolidine 4o (tangxj-4-165)

The reaction of 4 Å MS (3.0025 g), CuBr (0.0215 g, 0.15 mmol), 1a (1.0217 g, 10 mmol)/toluene (3 mL), 2h (1.0795 g, 11 mmol)/toluene (3 mL), and 3a (0.7821 g, 11 mmol)/toluene (4 mL) afforded 4o$^{[1]}$ (2.3526 g, 93%) (eluent: petroleum ether (200 mL); then petroleum ether/ethyl acetate = 200/1 (200 mL)→50/1 (200 mL)→5/1 (200 mL); finally petroleum ether/ethyl acetate/Et$_3$N = 700 mL/350 mL/1 mL was applied to get the pure product) as a liquid: 
$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.45-7.38 (m, 2 H, Ar-H), 7.30-7.21 (m, 3 H, Ar-H), 2.84-2.74 (m, 4 H, CH$_2$NCH$_2$), 2.07-1.98 (m, 2 H, 2×one proton of CH$_2$), 1.83-1.47 (m, 11 H, 5×CH$_2$ + one proton of CH$_2$), 1.30-1.17 (m, 1 H, one proton of CH$_2$); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 131.5, 127.9, 127.4, 123.5, 90.2, 85.9, 59.0, 46.8, 37.7, 25.5, 23.3, 22.8; MS (ESI) m/z 254 (M+H$^+$), 183 (M+H$^+$-pyrrolidine); IR (neat): $\nu$ = 2929, 2854, 2806, 1598, 1488, 1444, 1289, 1265, 1158, 1124, 1068 cm$^{-1}$; HRMS calcd for C$_{19}$H$_{27}$N [M$^+$]: 253.1830. Found: 253.1829.

(16) 4-(3-Methyl-1-phenylhept-1-yn-3-yl)morpholine 4p (tangxj-4-162)
The reaction of 4 Å MS (2.9979 g), CuBr (0.0215 g, 0.15 mmol), 1a (1.0217 g, 10 mmol) /toluene (3 mL), 2a (1.1017 g, 11 mmol)/toluene (3 mL), and 3b (0.9573 g, 11 mmol)/toluene (4 mL) afforded 4p (1.7343 g, 64%) (eluent: petroleum ether (200 mL); then petroleum ether/ethyl acetate = 200/1 (200 mL) → 100/1 (200 mL); finally petroleum ether/ethyl acetate/Et₃N = 900 mL/90 mL/1 mL was applied to get the pure product.) as a liquid: ¹H NMR (400 MHz, CDCl₃) δ 7.44-7.37 (m, 2 H, Ar - H), 7.30-7.22 (m, 3 H, Ar - H), 3.74 (t, J = 4.6 Hz, 4 H, CH₂OCH₂), 2.74-2.61 (m, 4 H, CH₂NCH₃), 1.74-1.65 (m, 2 H, CH₂), 1.51-1.40 (m, 2 H, CH₂), 1.40-1.28 (m, 5 H, CH₂ + CH₃), 0.94 (t, J = 7.2 Hz, 3 H, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 131.5, 128.0, 127.6, 123.2, 91.1, 84.5, 67.3, 57.6, 47.0, 38.7, 25.9, 23.6, 22.9, 14.0; MS (ESI) m/z 272 (M+H⁺), 185 (M+H⁺-morpholine - CH₃CH₂CH=CH₂); IR (neat): v = 2956, 2817, 1598, 1489, 1453, 1270, 1118 cm⁻¹; HRMS calcd for C₁₈H₂₅N⁰/O: [M⁺]: 271.1936. Found: 271.1928.

(17) 1-(3-Methyl-1-phenyleth-1-yn-3-yl)piperidine 4q (tangxj-5-23)

The reaction of 4 Å MS (301.0 mg), CuBr (14.1 mg, 0.1 mmol), 1a (204.2 mg, 2 mmol) /toluene (0.3 mL), 2a (99.5 mg, 1 mmol)/toluene (0.3 mL), and 3c (84.7 mg, 1 mmol)/toluene (0.4 mL) afforded 4q (142.9 mg, 53%) (eluent: petroleum ether (200 mL); then petroleum ether/ethyl acetate = 200/1 (200 mL) → 150/1 (200 mL) → 100/1 (200 mL) → 50/1) as a liquid: ¹H NMR (400 MHz, CDCl₃) δ 7.46-7.39 (m, 2 H, Ar - H), 7.31-7.24 (m, 3 H, Ar - H), 2.72-2.55 (m, 4 H, CH₂NCH₂), 1.77-1.68 (m, 2 H, CH₂), 1.66-1.58 (m, 4 H, 2 × CH₂), 1.52-1.29 (m, 9 H, 3 × CH₂ + CH₃), 0.93 (t, J = 7.2 Hz, 3 H, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 131.6, 128.1, 127.5, 123.7, 92.5, 83.9, 58.1,
47.7, 39.2, 26.6, 24.7, 23.9, 23.1, 14.1; MS (ESI) m/z 270 (M+H+), 185 (M+H+)-piperidine; IR (neat): ν = 2931, 2856, 2798, 1598, 1489, 1442, 1263, 1169, 1150, 1088, 1070, 1027 cm⁻¹; HRMS calcd for C₁₉H₂₇N [M⁺]: 269.2143. Found: 269.2138.

(18) 1-(2,4-Diphenylbut-3-yn-2-yl)pyrrolidine 4r (tangxj-5-19)

![Chemical structure of 4r](image)

The reaction of 4 Å MS (300.8 mg), CuBr (14.2 mg, 0.1 mmol), 1a (509.7 mg, 5 mmol)/toluene (0.5 mL), 2i (120.5 mg, 1 mmol)/toluene (0.5 mL), and 3a (83.5 μL, d = 0.852 g/mL, 71.1 mg, 1 mmol) afforded 4r (126.6 mg, 46%) (eluent: petroleum ether (200 mL); then petroleum ether/ethyl acetate = 200/1 (200 mL) → 150/1 (200 mL) → 100/1 (200 mL); finally petroleum ether/ethyl acetate/NH₃ = 900 mL /18 mL /0.5 mL was applied to get the pure product.) as a liquid: ¹H NMR (400 MHz, CDCl₃) δ 7.78 (d, J = 7.2 Hz, 2 H, Ar-H), 7.56-7.47 (m, 2 H, Ar-H), 7.39-7.20 (m, 6 H, Ar-H), 2.82-2.71 (m, 2 H, CH₂N), 2.67-2.55 (m, 2 H, NCH₂), 1.84-1.69 (m, 7 H, 2 × CH₂ + CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 145.6, 131.8, 128.2, 128.0, 127.9, 127.0, 126.3, 123.4, 89.4, 87.2, 62.5, 48.4, 32.3, 23.8; MS (ESI) m/z 276 (M+H⁺), 205 (M⁺-piperidine); IR (neat): ν = 1598, 1489, 1445, 1365, 1222, 1105, 1027, 1000 cm⁻¹; HRMS calcd for C₂₀H₂₁N [M⁺]: 275.1674. Found: 275.1670.

Reactions in benzene with a Dean-Stark trap in the absence of 4 Å molecular sieves.

(1) 1-(3-Methyl-1-phenylhept-1-yn-3-yl)pyrrolidine 4a (tangxj-5-128)

![Chemical structure of 4a](image)

**Typical Procedure 2:** To a three-necked flask equipped with a Dean-Stark trap and a condenser dried under vacuum with a heating gun were added CuBr (0.1073 g, 0.75
mmol), 1a (5.1077 g, 50 mmol)/benzene (20 mL), 2a (5.5095 g, 55 mmol)/benzene (20 mL), and 3a (3.9121 g, 55 mmol)/benzene (10 mL) sequentially under Ar atmosphere. The flask was then placed in a pre-heated oil bath of 110 °C with stirring for 3.5 h as monitored by TLC. After cooling to room temperature, the crude reaction mixture was filtrated through a short pad of silica gel eluted with acetone (200 mL). After evaporation, the residue was purified by chromatography on silica gel to afford 4a (11.7335 g, 92%) (eluent: petroleum ether (200 mL); then petroleum ether/ethyl acetate = 150/1 (200 mL)→70/1 (200 mL); finally petroleum ether/ethyl acetate/Et3N = 900 mL/180 mL/1 mL was applied to get the pure product.) as a liquid: 1H NMR (400 MHz, CDCl3) δ 7.44-7.38 (m, 2 H, Ar-H), 7.30-7.23 (m, 3 H, Ar-H), 2.84-2.73 (m, 4 H, C3H2NCH2), 1.84-1.62 (m, 6 H, 3 × CH2), 1.57-1.29 (m, 7 H, 2 × CH2 + CH3), 0.94 (t, J = 7.2 Hz, 3 H, CH3); 13C NMR (100 MHz, CDCl3) δ 131.5, 128.0, 127.4, 123.5, 91.3, 84.2, 57.7, 47.6, 41.1, 26.4, 25.7, 23.5, 23.0, 14.0.

(2) 2,5-Dimethyl-5-(pyrrolidin-1-yl)non-3-yn-2-ol 4g (tangxj-5-138)

Following the above procedure, the reaction of CuBr (0.1079 g, 0.75 mmol), 1g (4.2071 g, 50 mmol)/benzene (20 mL), 2a (5.5095 g, 55 mmol)/benzene (20 mL), and 3a (3.9122 g, 55 mmol)/benzene (10 mL) afforded 4g (11.3311 g, 95%) (eluent: petroleum ether (200 mL); then petroleum ether/ethyl acetate = 50/1 (200 mL)→1/1 (200 mL); finally petroleum ether/ethyl acetate/Et3N = 180 mL/900 mL/1 mL was applied to get the pure product.) as a solid: 1H NMR (400 MHz, CDCl3) δ 2.74-2.61 (m, 4 H, CH2NCH2), 2.52 (br s, 1 H, OH), 1.82-1.72 (m, 4 H, 2 × CH2), 1.70-1.49 (m, 8 H, CH2 + 2 × CH3), 1.43-1.26 (m, 7 H, 2 × CH2 + CH3), 0.91 (t, J = 7.2 Hz, 3 H, CH3); 13C NMR (100 MHz, CDCl3) δ 89.1, 83.1, 64.9, 57.1, 47.5, 41.0, 32.02, 31.99, 26.4, 25.7, 23.5, 23.0, 14.0.
Reference: